

## Genetic markers may help predict fertility decline in women

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(Medical Xpress) -- Researchers at the Stanford Institute for Stem Cell Biology and Regenerative Medicine have discovered genetic markers that may ultimately allow women to track and predict declining fertility.

The study, which was published in the February issue of Human Reproduction, found three particular gene variants that could be associated with the age of onset of fertility decline.

Ultimately, this study and further research may allow individual women to know in advance the approximate age when their fertility will decline, allowing them to plan accordingly.

"Many women now are delaying childbirth until their mid to late 30s, which is getting very near the edge of the usual fertility window," said first author Sonya Schuh-Huerta, PhD, a postdoctoral scholar. Some of these women are destined to have diminished fertility by the time they try to have children, but they won't know that in advance, Schuh-Huerta said.

Testing for the number of maturing eggs in the ovary and levels of reproductive hormones can be a good indication of fertility, but women tend not to get these tests until they are already experiencing difficulties with conceiving. "Ultimately, a test for specific genetic markers would be easier and could give them more information and more power to make reproductive decisions," Schuh-Huerta said.



The age of onset of menopause is highly determined by genetics, a fact that many women don't know, said senior author Renee Reijo Pera, PhD, professor of obstetrics & gynecology. "We did a survey of undergraduates and most didn't realize that their reproductive biology is relatively fixed," she said. "They thought that if they didn't smoke, ate right and exercised they could extend their fertile years."

Reijo Pera and her colleagues set out to search for those genes that would indicate early or late menopause. They recruited healthy women of reproductive age, took DNA samples, and tested the women for levels of reproductive hormones, which is one indicator of fertility. Then they cast a wide net, sorting through all the genes in the body in what is called a genome-wide association study to find those genes that were associated with early declines or rises in reproductive hormones. The study looked for these results in Caucasian and African American women to make sure that any genetic findings were valid in very different populations.

"Normally, to test for fertility you can do a hormone assay and get a number, but if you talk to the heads of in-vitro fertilization clinics, they'll say that hormone levels are highly variable," said Reijo Pera. "We know when the hormones really crash that shows a decline in fertility, but there is a wide swath of hormone levels where we just don't know exactly what they mean."

The researchers hope that the new gene markers will help them better gauge fertility and interpret the hormonal tests. Interestingly enough, the genes discovered to be associated with <u>reproductive hormones</u> previously had no known connection to <u>human reproduction</u>, Schuh-Huerta says. "Some of them are active in early development, so they may have something to do with formation of early germ cells [eggs]," she said.

If a genetic test for fertility is developed, it could also help predict the



likelihood of other health problems, since declining ovarian function is associated with cardiovascular problems, bone mineralization diseases (including osteoporosis) and various cancers, Schuh-Huerta said. And because such genes are present one's whole life, clinicians would be able to make predictions about fertility and other health problems decades in advance.

The researchers are currently finishing a study that looks for genes associated with the number of viable egg follicles in the ovaries, which is another good indicator of fertility. Other than information gained through studies in animal models, very little is known about genes directly linked with the number of eggs in the human ovary.

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